The Examiner has noted that this application has been filed with informal drawings, which are acceptable for examination purposes only. Formal drawings will be provided upon an indication of allowability of the application.

The Examiner has required amendment of the specification to recite the status of parent application Serial No. 08/367,507, and to provide a brief description of Figures 6 and 7. The Application has been amended accordingly. Support for the recitation of the brief description of Figures 6 and 7 is found in the figures as filed.

The Specification Describes and Enables the Claimed Invention

The Examiner has rejected claims 1-9 and 30 under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention. The specification refers to an antibody 4G9 by ATCC accession number. The Examiner has required that Applicants provide an affidavit or declaration stating that the hybridoma cell line has been deposited under the Budapest Treaty and that the hybridoma cell line will be irrevocably and without restriction or condition released to the public upon the issuance of a patent to satisfy the deposit requirement.

In response, Applicants note that the hybridoma producing monoclonal antibody 4G9 has been deposited with the American Type Culture Collection (ATCC), 12301 Parklawn Drive, Rockville, Maryland 20852 on April 27, 1994 under the provisions of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure, and was assigned accession number CRL 11626. A copy of the deposit

receipt is attached hereto as Exhibit A. Furthermore, compliance with the provisions of 37 C.F.R. § 1.801 *et seq.* is assured in the accompanying Declaration of Veronica Mallon, Ph.D., Vice-President, Scientific Communications and Intellectual Property of Alteon Inc., the depositor and assignee of the entire right, title, and interest in, to, and under this application. In particular, Dr. Mallon declares that in accordance with the Budapest Treaty and the Patent Laws and Rules, (a) during the pendency of this application, access to the deposit will be afforded to the Commissioner upon request; (b) all restrictions upon the availability to the public of the deposited biological material will be irrevocably removed upon the granting of a patent on this application; (c) the deposit will be maintained in a public depository for a period of at least thirty years from the date of deposit or for the enforceable life of the patent or for a period of five years after the date of the most recent request for the furnishing of a sample of the deposited biological material, whichever is longest; and, (d) the deposit will be replaced if it should become nonviable or non-replicable.

In view of the foregoing remarks, Applicants submit that the Examiner's rejection is obviated and should be withdrawn.

Particularity and Distinctiveness of the Claims

The Examiner has rejected claims 1-9 and 30 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite.

The Examiner contends that the recitation of the "immunological binding characteristics of monoclonal antibody 4G9" is vague and indefinite. Applicants respectfully disagree, and direct the Examiner's attention to the specification at page 11, line 32 to page 12, line 2, which defines the allegedly indefinite term. The specificity, affinity, cross-

reactivity, and other binding characteristics of the antibody are readily determined using routine procedures, including but not limited to those set out on page 14, line 19 to page 15, line 10. In particular, by identifying an antibody that competitively inhibits the deposited 4G9 antibody, one of ordinary skill in the art clearly identifies an antibody with binding characteristics of the 4G9 monoclonal antibody. Binding characteristics of 4G9 are set forth in the Examples, at page 24, line 9 to page 26, line 7, and in particular in Table 1 on page 26. Thus, contrary to the Examiner's allegations, the specification does describe immunological binding characteristics of the deposited strain, and the metes and bounds of claims 1-5, 7, and 8 can be readily determined.

The Examiner states that the labeled antibody recited in claim 7 has no antecedent basis in claim 1. In response, Applicants respectfully point out that claim 7 refers to an antibody of claim 1 which is labeled. Thus, it correctly includes a further limitation of the antibody or fragment thereof of claim 1.

The Examiner has identified some confusing language in claim 9. In response, Applicants have amended claim 9 to delete the confusing language.

The Examiner states that the term "monoclonal antibody" in claim 6 has no antecedent basis in claim 4. In response, Applicants have amended claim 6 to depend from claim 5.

In view of the foregoing amendments and remarks, Applicants submit that the Examiner's rejection is obviated in part and overcome in part, and should be withdrawn.

The Claimed Invention Is Non-obvious

The Examiner has rejected claims 1, 2, 4-9 and 30 under 35 U.S.C. § 103(a) as being

unpatentable over Makita et al. [*J. Biol. Chem.* (1992)] or Makita et al. [*Science* (1992)] (hereinafter, collectively, "Makita" as both references refer to the same polyclonal anti-AGE-RNase antibody; *see* The Declaration of Henry Founds, Ph.D. Under 37 C.F.R. § 1.132 (Founds Declaration)) in view of Harlow et al. [*Antibodies* (1988)]. The Examiner has rejected claim 3 under 35 U.S.C. § 103(a) as being allegedly unpatentable over the foregoing references in view of Queen et al. [*Proc. Natl. Acad. Sci. USA* (1989)]. Because the primary references fail to suggest, much less teach, an anti-AGE antibody having the properties of 4G9, and the secondary references, which are silent with respect to anti-AGE antibodies, do not supply the missing teaching, both rejections are addressed here.

Applicants respectfully traverse the Examiner's rejection. As shown in the accompanying Founds Declaration, Makita does not teach a monoclonal antibody having the unexpected combination of characteristics of 4G9. The monoclonal antibody of the present invention improves upon the Makita antibody. Dr. Founds states that although the Makita antibodies have the properties demonstrated by the claimed monoclonal, there is no way to predict which, if any, of these properties will predominate in a particular monoclonal, to what degree the monoclonal will evidence such properties, and what advantages these properties may confer (Founds Declaration, ¶5d). The teachings of Makita did not lead and would not have led Dr. Founds to develop a monoclonal having the characteristics of the 4G9 monoclonal of this application, which has high specificity for carboxymethyllysine, greater affinity for BSA-AGE in a thiocyanate comparative affinity assay, and greater sensitivity for AGEs on serum peptides and in skin than the antibodies described by Makita (*ibid*). Thus, although the claimed monoclonal is a species of Makita antibody, it is in Dr. Found's scientific opinion a distinct species that merits individual protection (*ibid*). Indeed,

the Examiner appears to agree with this point.

Neither Harlow nor Queen, whether taken alone or in combination, supplies the missing teaching. Applicants are in agreement with the Examiner with respect to the general teachings of Harlow with respect to monoclonal antibodies (see the specification at page 13, line 4 to page 14, line 17). Applicants agree that humanized or chimeric monoclonal antibodies have been described previously (specification, page 13, lines 13-32). However, neither Harlow nor Queen suggests, much less teaches, an AGE-specific monoclonal antibody. Accordingly, neither reference can be deemed to suggest an AGE-specific monoclonal antibody having the immunological binding characteristics of the monclonal of the invention.

A finding of obviousness under § 103 requires a determination of the scope and content of the prior art, the level of ordinary skill in the art, the differences between the claimed subject matter and the prior art, and whether the differences are such that the subject matter as a whole would have been obvious to one of ordinary skill in the art at the time the invention was made. *Graham* v. *Deere*, 383 U.S. 1 (1966). The relevant inquiry is whether the prior art suggests the invention and whether the prior art provides one of ordinary skill in the art with a reasonable expectation of success. *In re O'Farrell*, 7 USPQ 2d 1673 (Fed. Cir. 1988). Both the suggestion and the reasonable expectation of success must be founded in the prior art and not in the Applicant's disclosure. *In re Vaeck*, 20 USPQ 2d 1438 (Fed. Cir. 1991).

In the present instance, the proper inquiry involves whether the cited references suggest the claimed monoclonal antibody. As discussed in detail, above, the cited references do not suggest or provide a reasonable expectation of success of obtaining an antibody having

the immunological binding characteristic of 4G9, much less that it could b used to detect AGEs. The only suggestion of a monoclonal antibody having immunological binding characteristic of 4G9 is found in the instant disclosure. Thus, any rejection for obviousness must be improperly based on hindsight gained from the instant disclosure.

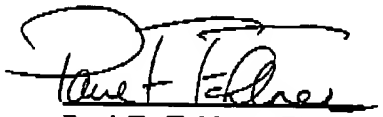
In view of the foregoing amendments and remarks, Applicants submit that the Examiner's rejection is obviated and should be withdrawn.

CONCLUSION

Applicants respectfully request entry of the foregoing amendments and remarks in the file history of the instant Application. The claims as amended are believed to be in condition for allowance, and reconsideration and withdrawal of all of the outstanding rejections is therefore believed in order. Early and favorable action on the claims is earnestly solicited.

Respectfully submitted,

KLAUBER & JACKSON



Paul F. Fehlner, Ph.D.
Attorney for Applicant(s)
Registration No. 35,135

KLAUBER & JACKSON
411 Hackensack Avenue
Hackensack NJ 07601
Tel: (201) 487-5800